Appl. No.: 10/720,662
Amdt. dated 09/27/2005
Reply to Office action of 06/27/2005

REMARKS/ARGUMENTS

As described below, Claims 9 and 16 have been amended to clarify the invention without raising new issues. As such, the amendments should be substantively considered at the juncture and pending rejection should be overcome. Claims 6-8 have been canceled. Based on the foregoing amendments and the following remarks, Applicant respectfully requests reconsideration of the present application and allowance of the pending set of claims.

35 U.S.C. §§ 101, 112, first paragraph

Claims 14-18 have been rejected under 35 U.S.C. § 101 as not being supported by either an operable utility or a well established utility. Claims 14-18 have also been rejected under 35 U.S.C. § 112, first paragraph, because the Examiner asserts that the Specification does not reasonably provide enablement for any transformant comprising a vector encoding any pre-S encoding nucleic acid. Claim 9 has been amended to recite that the recombinant pIL20-pre-S vector is capable of expression of pre-S without linkage to S protein. Claims 14-18 which are dependent on Claim 9 would therefore exclude inoperable and non-enabled embodiments that are not capable of being secreting the mutant pre-S. Accordingly, the rejection of Claims 14-18 under 35 U.S.C. §§ 101, 112, first paragraph, has been overcome.

35 U.S.C. § 103(a)

The Examiner has maintained the rejections of Claims 6-12 and 14-18 as being unpatentable over the cited references. Specifically, the Examiner asserts that the Applicant relies on elements not recited in the claims to distinguish the claimed invention. To further distinguish the claimed invention, Claim 9 has been amended to recite that the recombinant pIL20-pre-S vector is "capable of expression of pre-S without linkage to S protein." Accordingly, the claims are distinguished from the references because the references fail to teach or suggest the claimed gene, vector, or transformant that causes the expression of the modified pre-S without linkage to the S protein. In addition, Claims 6-8 have been canceled, thereby mooting the rejection of these claims.

As previously discussed, the claimed invention relates to a recombinant pIL20-pre-S vector with a nucleic acid sequence that codes for mutant pre-S (Claims 9 – 12), and a yeast transformant, where the transformant secretes a mutant pre-S (Claims 14 – 18). The gene,

vector, and transformant of the invention code for a pre-S that comprises the whole region of pre-S1 and pre-S2, but that is not linked to the S protein.

Kniskern relates to the expression of the HBV envelope protein having the whole region of pre-S2 and S proteins (the small form of HBV envelope protein). Comberbach relates to the expression of the HBV L protein or modified L protein consisting of the pre-S and S proteins. Thus, both Kniskern and Comberbach teach the expression of proteins that include S proteins, while the claimed gene, vector, and transformant express pre-S without the related S proteins. The remaining references fail to cure the deficiencies of Kniskern or Comberbach, i.e. they do not suggest the modification of Kniskern or Comberbach such that the expression of a pre-S would not be linked with the S protein.

The Claims are also distinguished from the cited references because the results obtained by expression of the pre-S proteins without the S protein are significant and altogether unexpected in view of the references. For the first time, the claimed invention has successfully expressed the pre-S protein without S protein. An adjuvant activity of the recombinant pre-S protein has been demonstrated, and that activity can be used to improve the immunogenicity of S antigen. The improved immunogenicity is an unexpected benefit over the disclosure of the references. Further, the finding that the replacement of the glycosylation sites of the pre-S with other amino acids, thereby eliminating glycosylation of pre-S, confers the pre-S with an activity that stimulates the immunogenicity of other HBV envelope antigens, rather than an improved immunogenicity of the pre-S itself (see Example 10). The finding that pre-S has an adjuvant activity is not suggested by the references.

The references further fail to teach or suggest the expression of the pre-S protein in a secreted form using a yeast expression system as recited in Claims 14 - 18. The claimed invention demonstrates not only the first successful expression of the recombinant pre-S protein (including both pre-S1 and pre-S2) in secreted form but also the first successful expression of the entire pre-S alone at such a high level (>200 mg/L). The claimed invention enables one to produce the pre-S portion of the HBV envelope protein on a large scale and describes the finding of the utility of pre-S as an adjuvant for the first time.

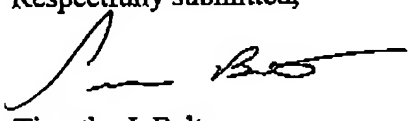
In conclusion, the claimed invention has, for the first time, described the expression of the pre-S protein of HBV, unlinked to the S protein, the expression of pre-S protein using a recombinant pIL20-pre-S vector, and a yeast transformant that expresses a pre-S in the secreted

form. The claimed invention has also demonstrated the unexpected function of the recombinant pre-S protein as an immunological adjuvant to stimulate the immunogenicity of S antigen, and the secretion and high expression level of the pre-S protein described in the claimed invention provide the condition for large scale production of the pre-S for industrial purposes. For these and the other reasons stated above, it is submitted that Claims 9 – 12 and 14 – 16 are patentable over the references, and it is respectfully submitted that the rejections under 35 U.S.C. 101, 112, and 103(a) have been overcome.

In view of the amendments and remarks made above, Applicant submits that the pending Claims are now in condition for allowance. Applicant respectfully requests that the claims be allowed to issue. If the Examiner wishes to discuss the application or the comments herein, the Examiner is urged to contact the undersigned by telephone.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



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I hereby certify that this paper is being facsimile transmitted to the US Patent and Trademark Office at Fax No. (571) 273-8300 on the date shown below.

Grace R. Rippy

September 27, 2005
Date